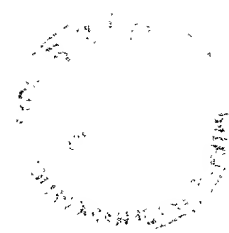


Primary lymphedema (clinical classification).

Diagnosis	Frequency ^{22,31,32,39} (% of all primary forms)
<i>Congenital (onset <2 years after birth)</i>	6-12
Familial, autosomal dominant (Nonne-Milroy disease)	
Familial, non-dominant inheritance	
Sporadic (most common congenital form)	
<i>Lymphedema precox (onset between 2-35 years)</i>	77-94
Familial, autosomal recessive (Meige disease)	
Sporadic (83-94% of all lymphedema precox)	
<i>Lymphedema tarda (onset after 35 years of age)</i>	11

FIG. 1A

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Functional Classification of Primary Lymphedema			
	Distal Obliteration (80%)	Proximal Obliteration (10%)	Hyperplasia* (10%)
Gender	Female	Male orFemale	Male orFemale
Onset			
Time	Puberty	Any age	Congenital
Location	Ankle; bilateral	Whole leg, thigh; unilateral	Whole leg; unilateral or bilateral
Progression	Slow	Rapid	Progressive
Family history	Frequently positive	None	Frequently positive

FIG. 1B



Secondary lymphedema

Blockade at the level of the lymph node

- Regional lymph node dissection
 - Axillary (post-mastectomy lymphedema)
 - Pelvic and para-aortic (leg and groin lymphedema)
 - Neck (head and neck lymphedema)
- Neoplastic disease
 - Hodgkin lymphoma
 - Metastatic cancer
 - Prostate cancer
 - Cervical cancer
 - Breast cancer
 - Melanoma

Disruption or obliteration of lymphatic channels

- Surgery, e.g. ilio-femoral bypass
 - Direct injury, e.g. trauma of the medial aspect of the thigh
 - Radiation-induced fibrosis
 - Neoplastic infiltration of lymphatic channels
 - Rheumatoid arthritis
 - Filariasis
 - Recurrent infection, e.g. erysipelas
-

FIG. 1C

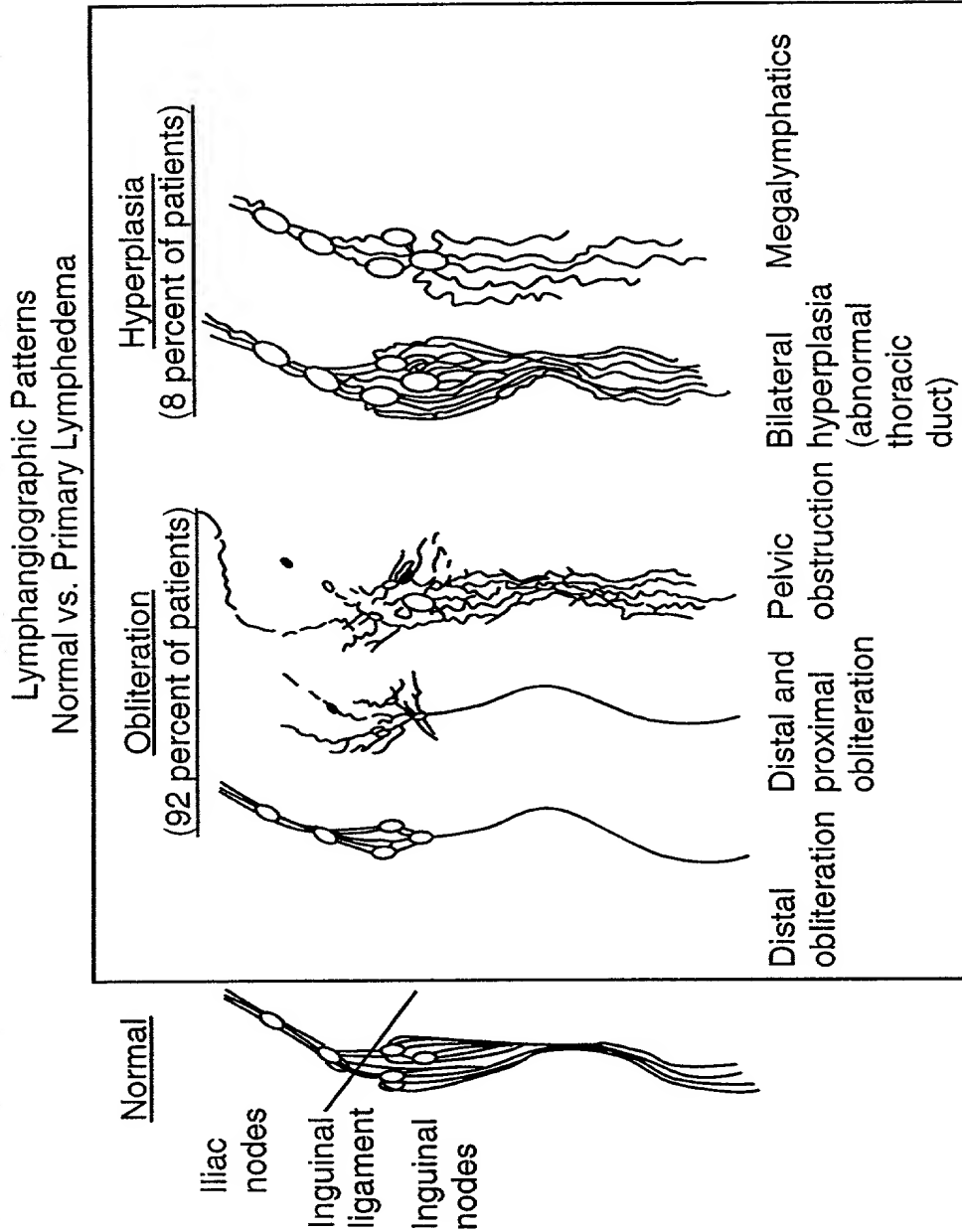
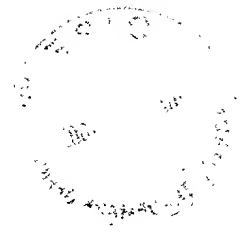


FIG. 2



Rabbit Ear Lymphedema Model
Clinical Appearance — 5Month



VEGF-2

Control

FIG. 3

205090" 8800/560

6/35

Rabbit Ear Lymphedema Model
Lymphoscintigraphy — 5 Month Post-Op

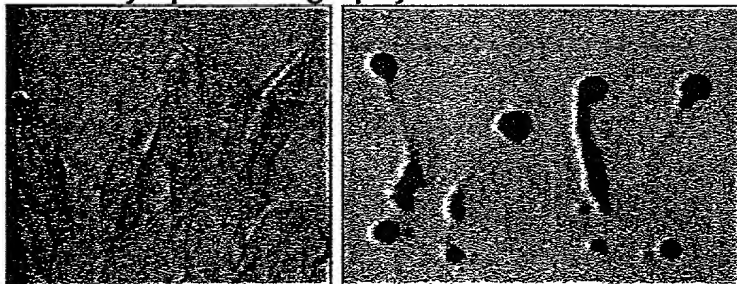
VEGF-2

Control



FIG. 4

Rabbit Ear Lymphedema Model
Lymphoscintigraphy — Orientation

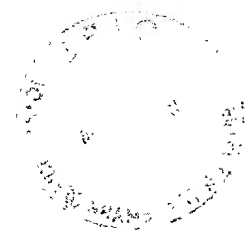


Right
Operated

Left
Normal

FIG. 5

7/35



Rabbit Ear Lymphedema Model
Lymphoscintigraphy — Early Post-Op

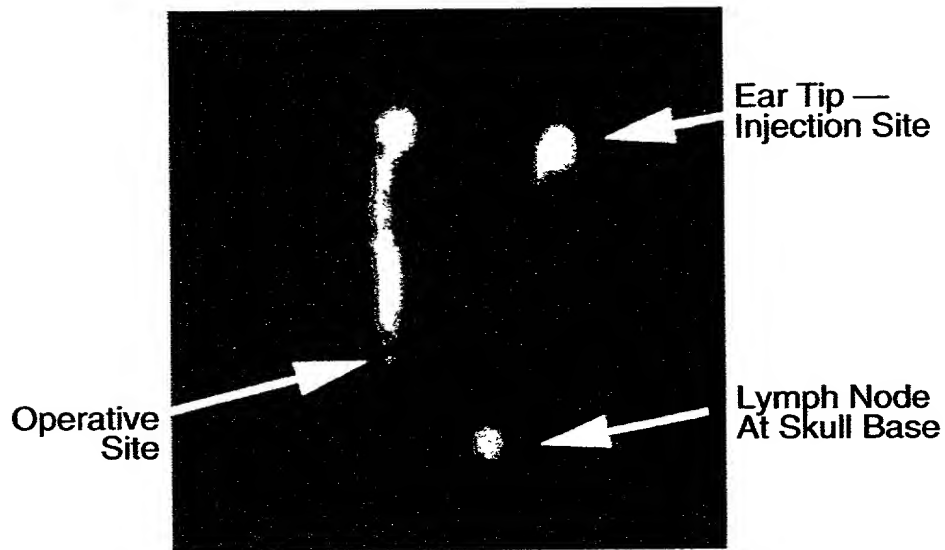


FIG. 6

205330 2300 660

8/35

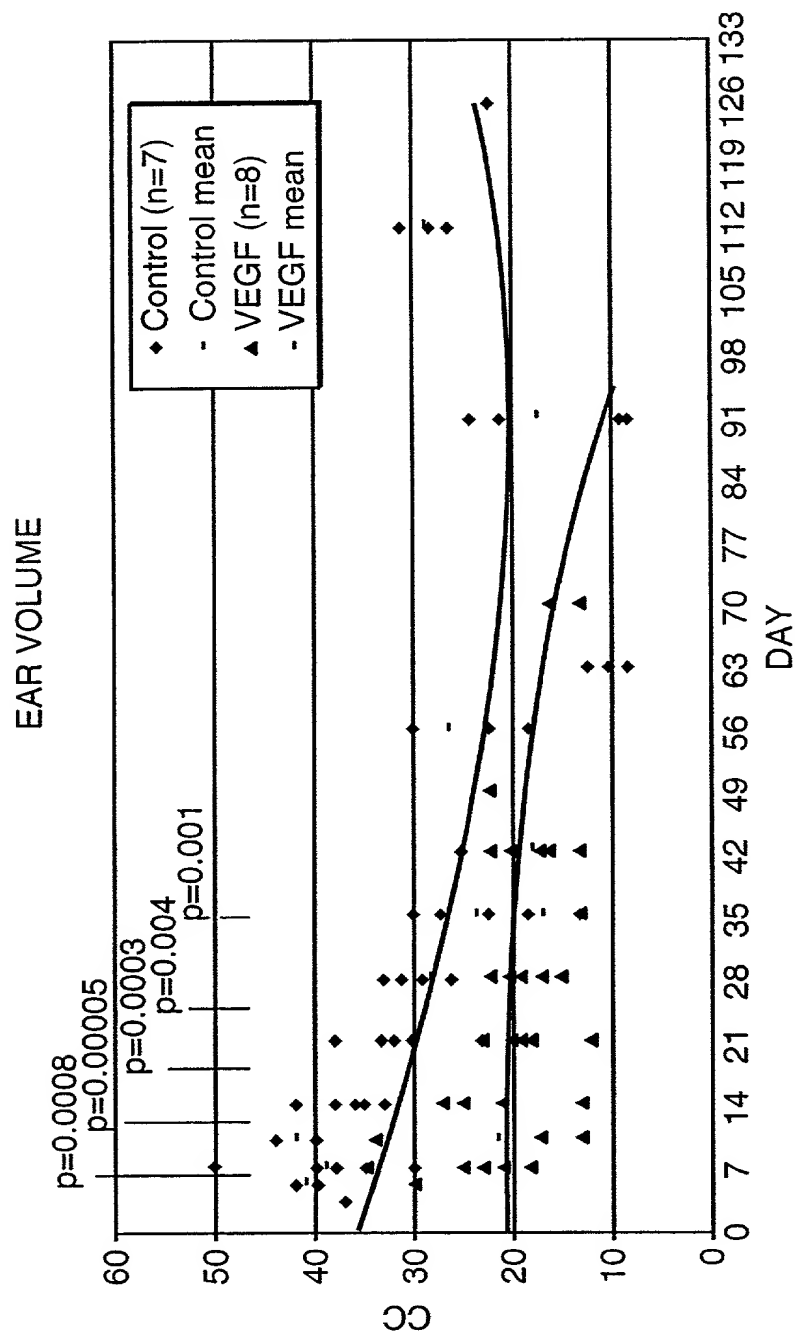


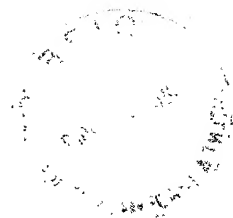
FIG. 7

1000
 900
 800
 700
 600
 500
 400
 300
 200
 100
 0

A high-contrast, black and white photograph of a person's face, heavily shadowed and grainy, with bright highlights on the forehead and cheek. The image is oriented vertically.

$$\frac{F}{G} \propto \frac{1}{G}$$

10/35



Human Lymphoscintigraphy
Right Lower Extremity

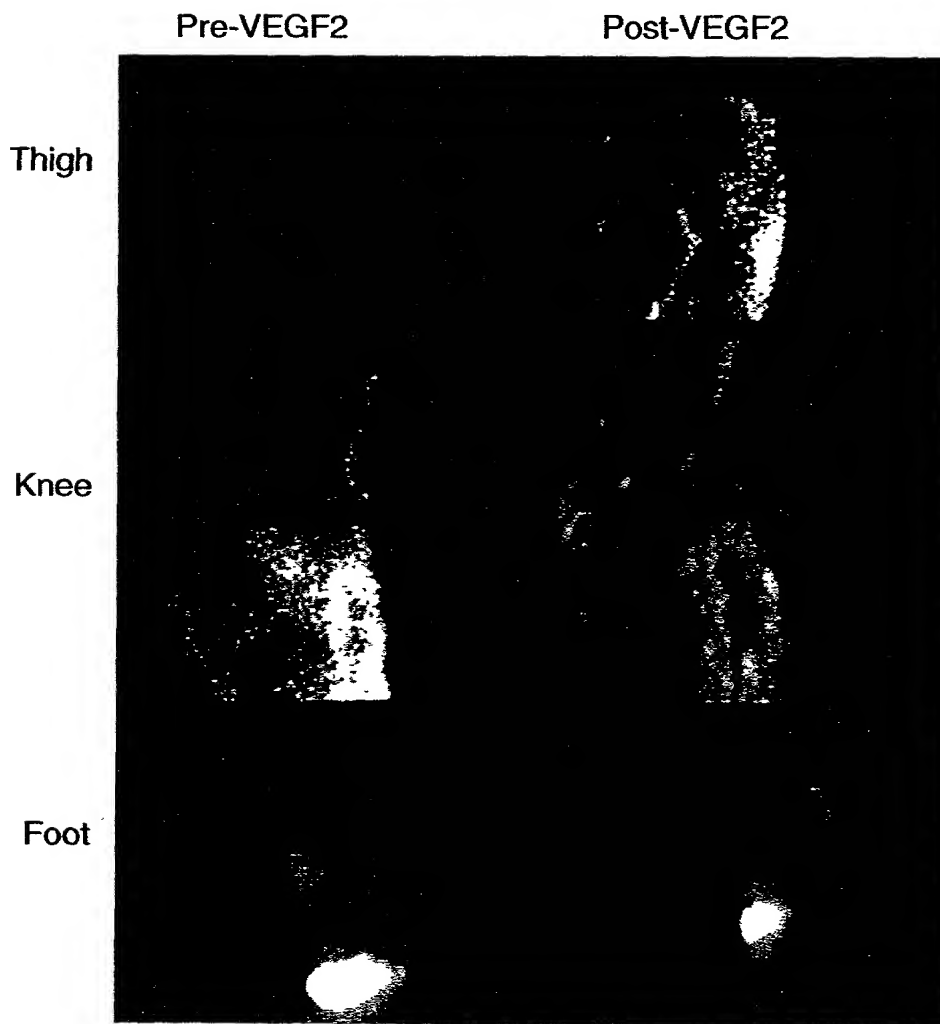


FIG. 9

205099 00000000

11/35

Ultrasound Imaging of Intra-Muscular
VEGF-2 Gene Transfer: Lymphedema

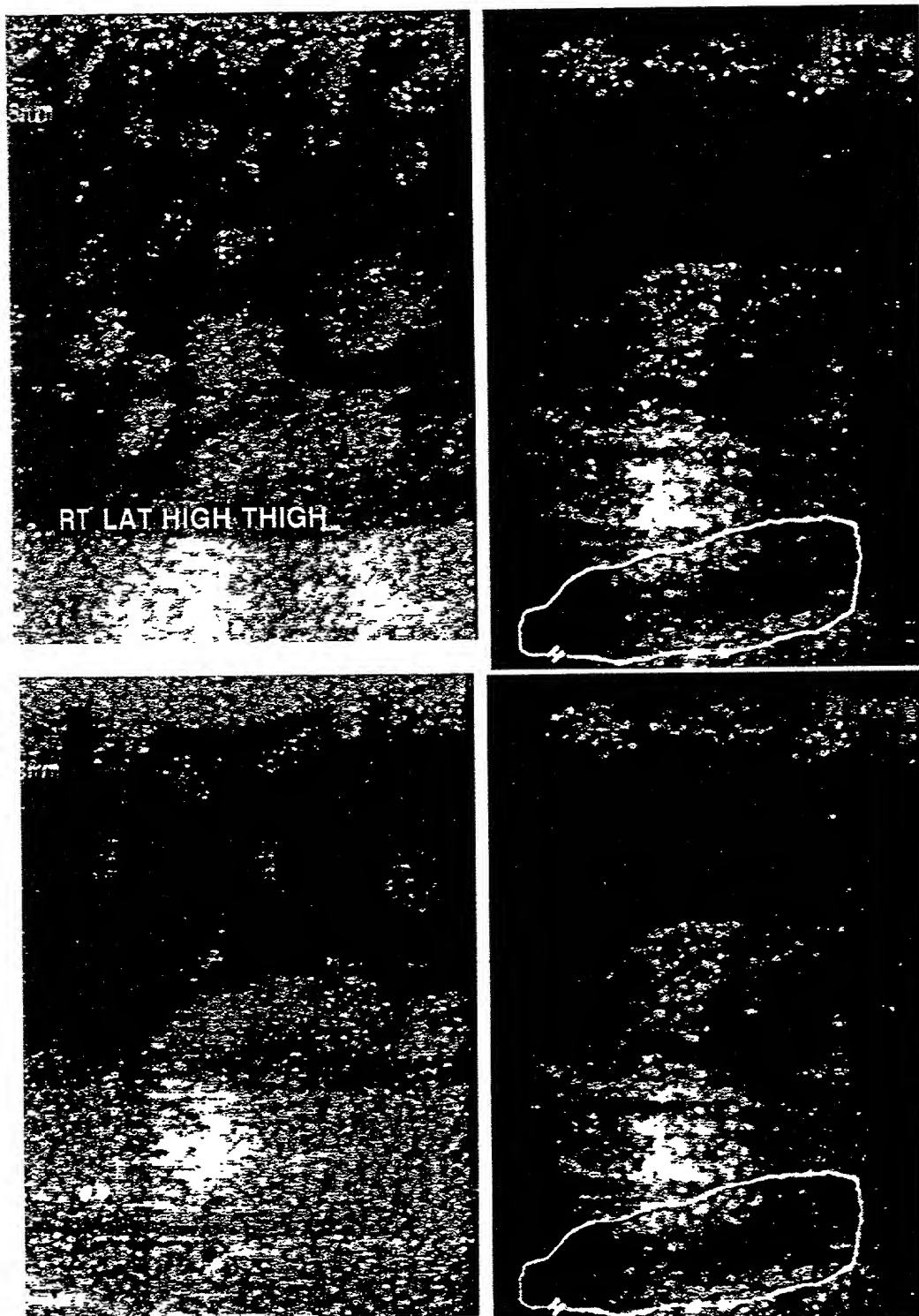


FIG. 10

205090-8800/650

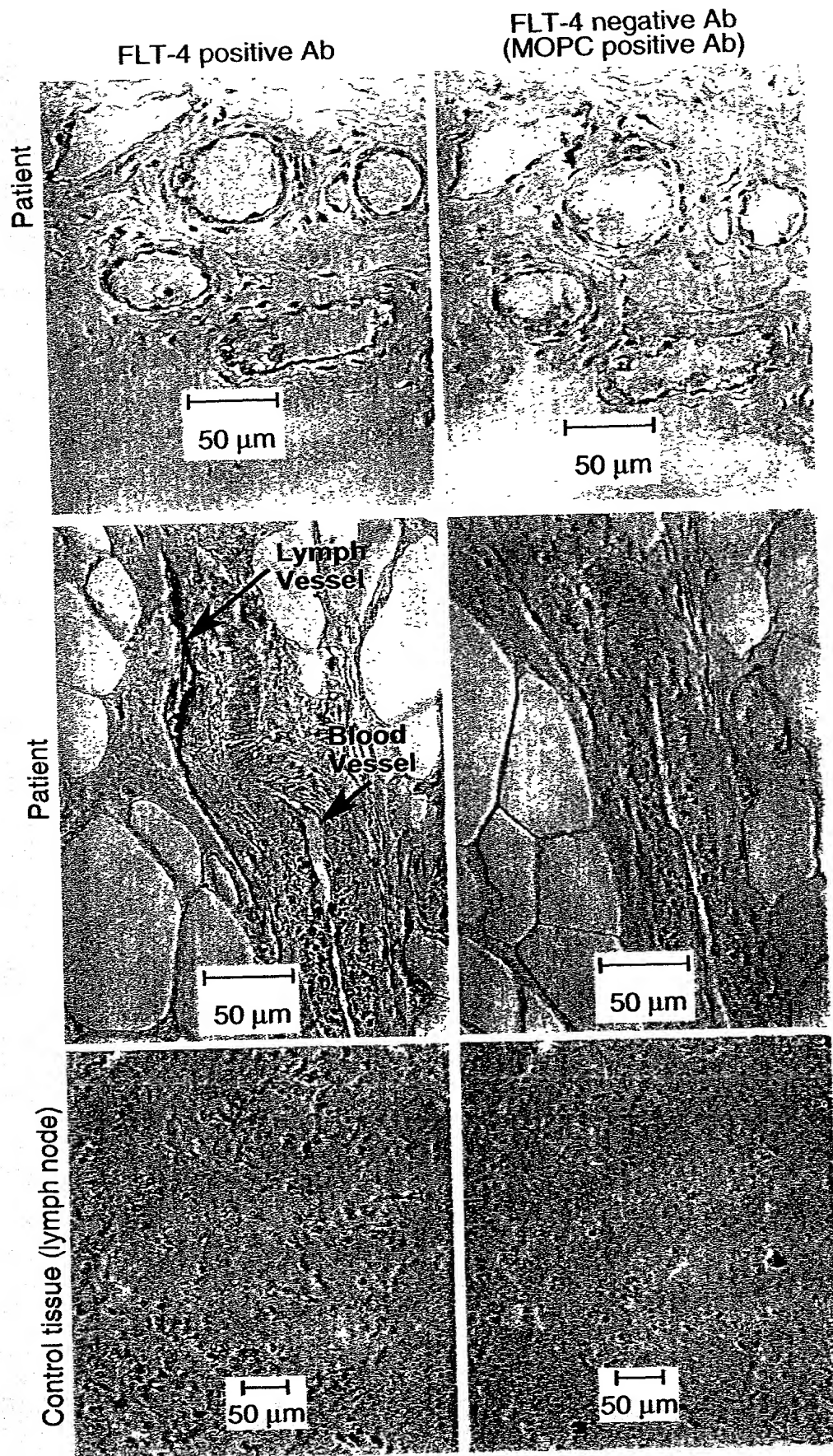


FIG. 11



FIG. 12B



FIG. 12A

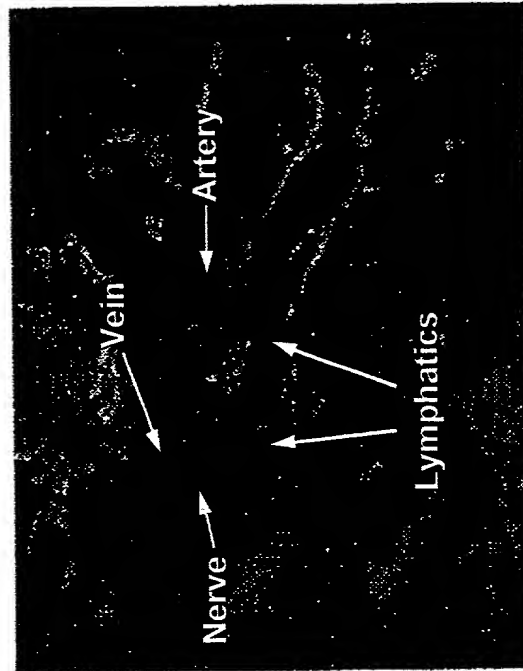


FIG. 12C

205000 8800 650

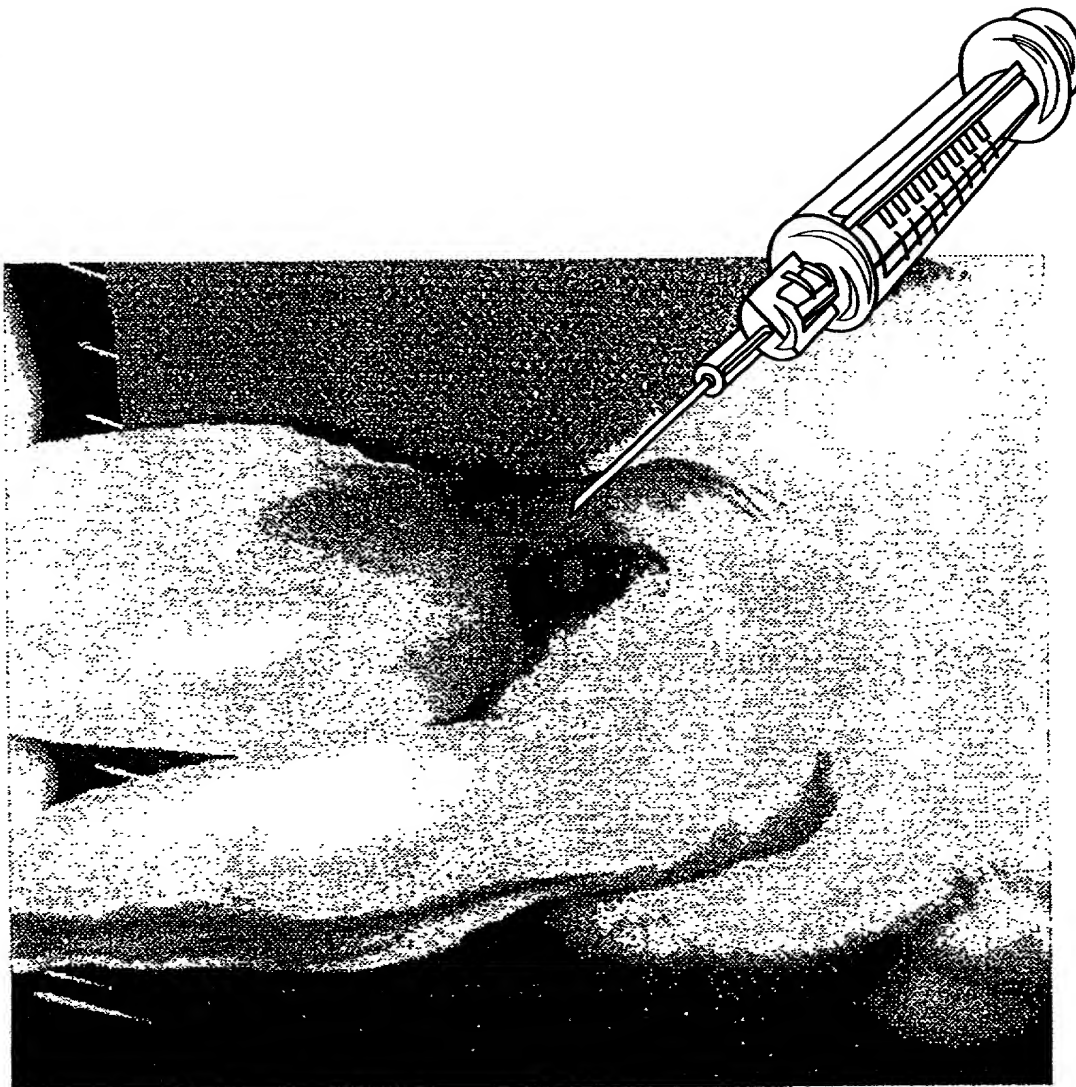


FIG. 13A

09/000000 00000000

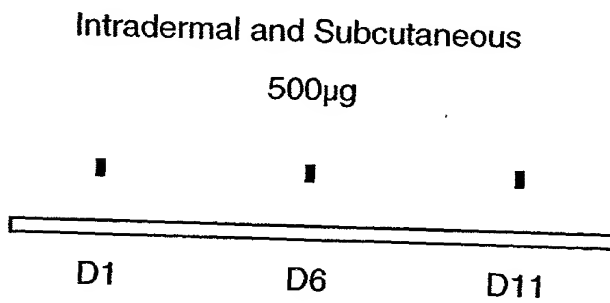


FIG. 13B



FIG. 14A



FIG. 14B

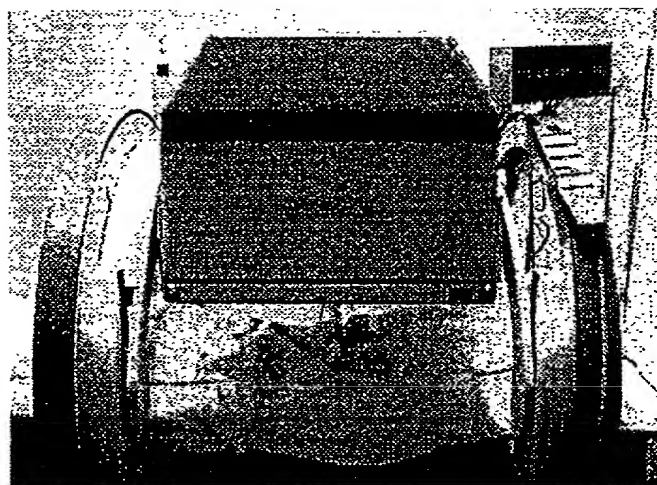
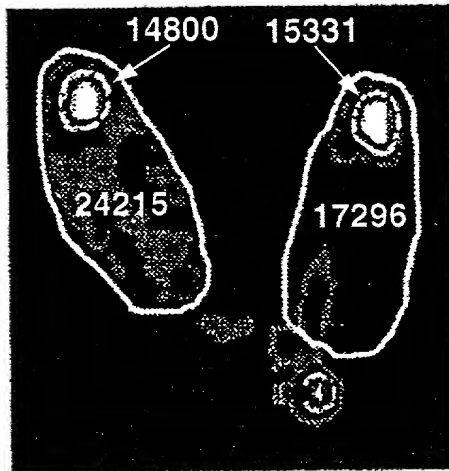


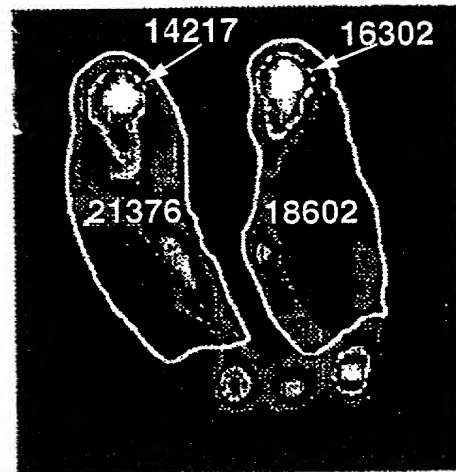
FIG. 14C

09/970,088



$$(24125-14800)/(17296-15331) = 4.75$$

FIG. 15A



$$(21376-14217)/(18602-16302) = 3.11$$

FIG. 15B

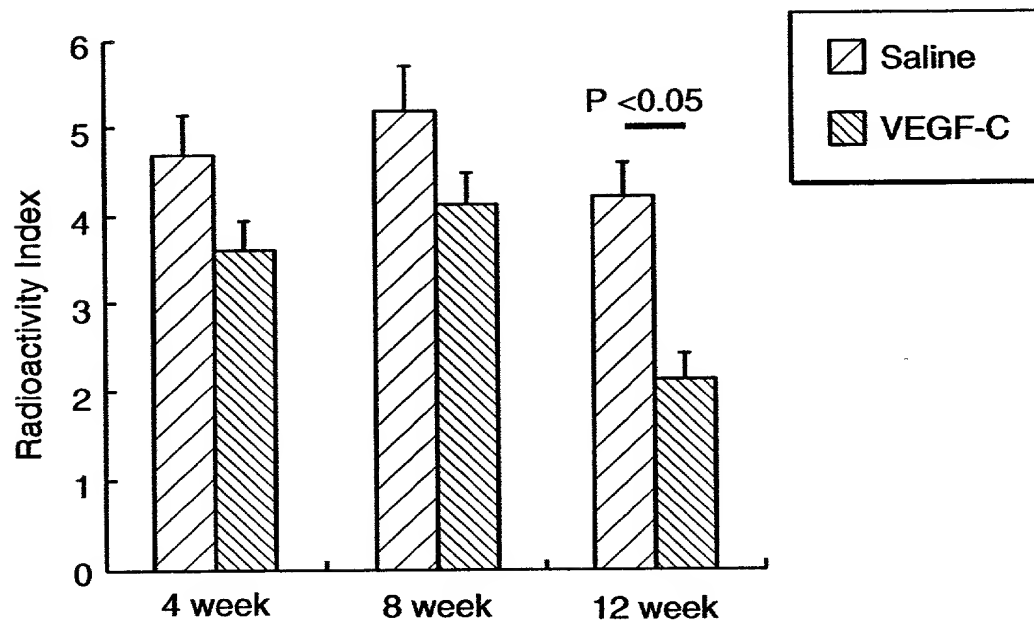


FIG. 15C

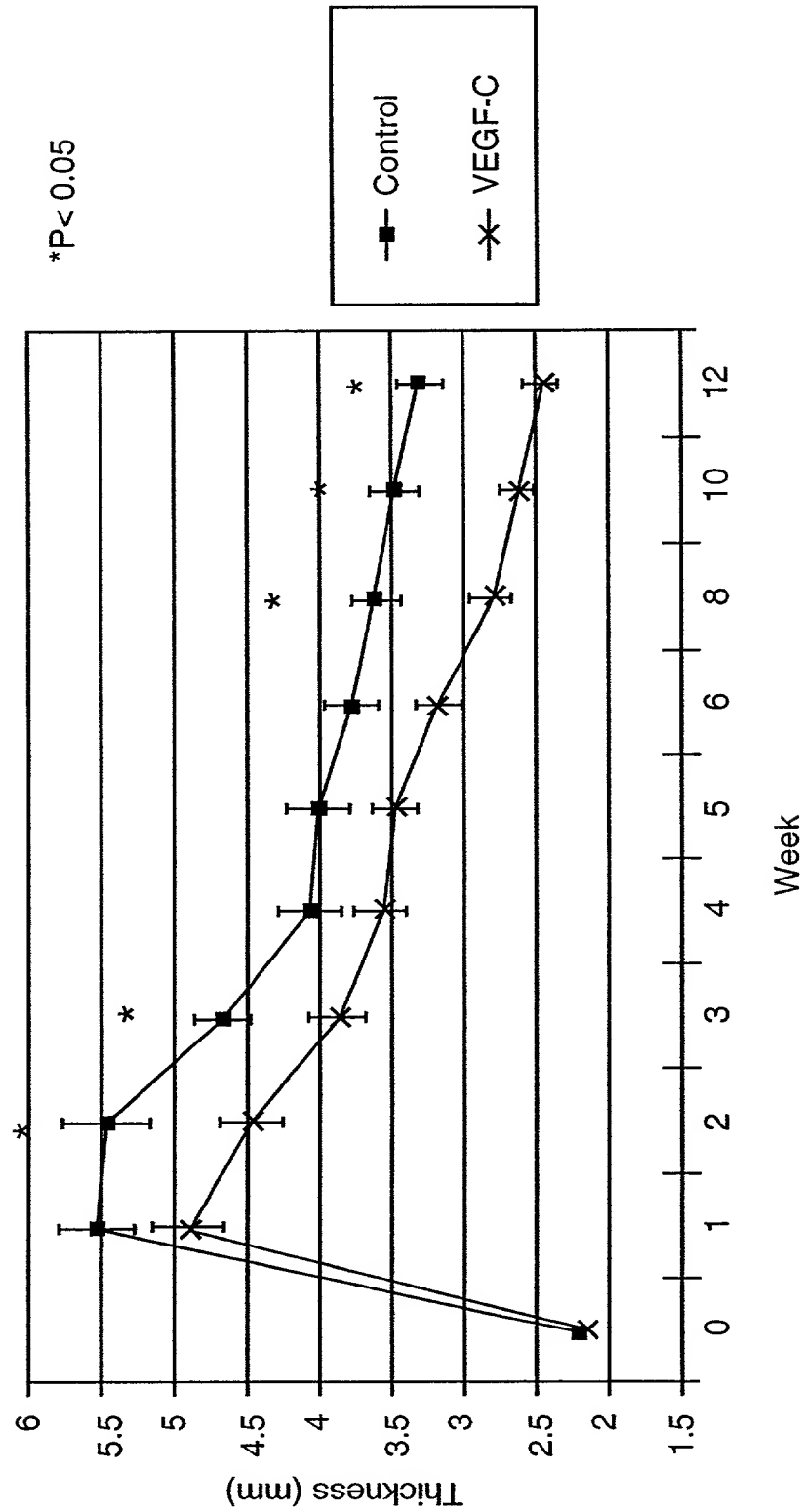
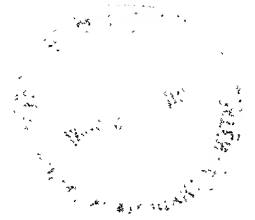


FIG. 16A

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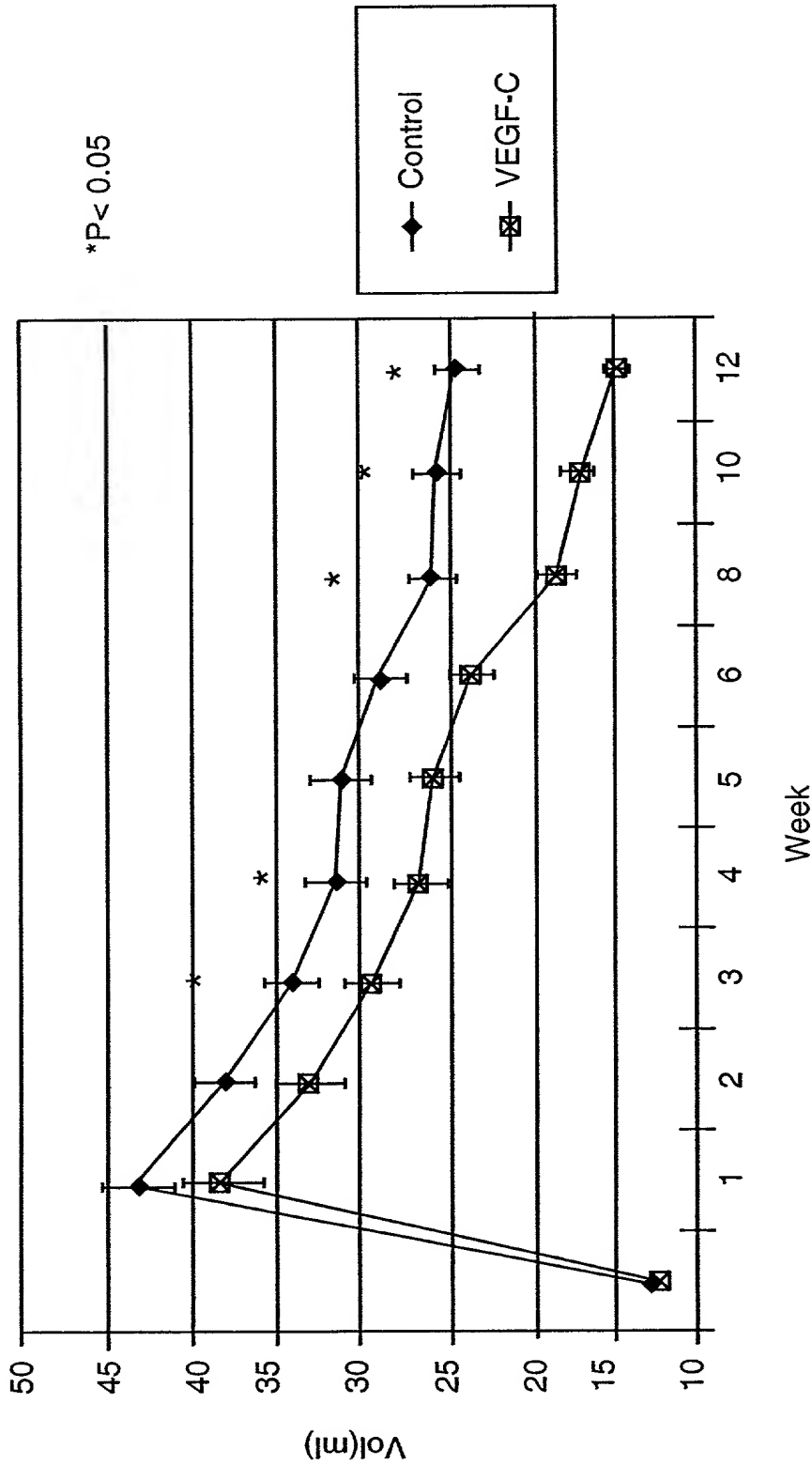


FIG. 16B



FIG. 17A

Control



VEGF-C

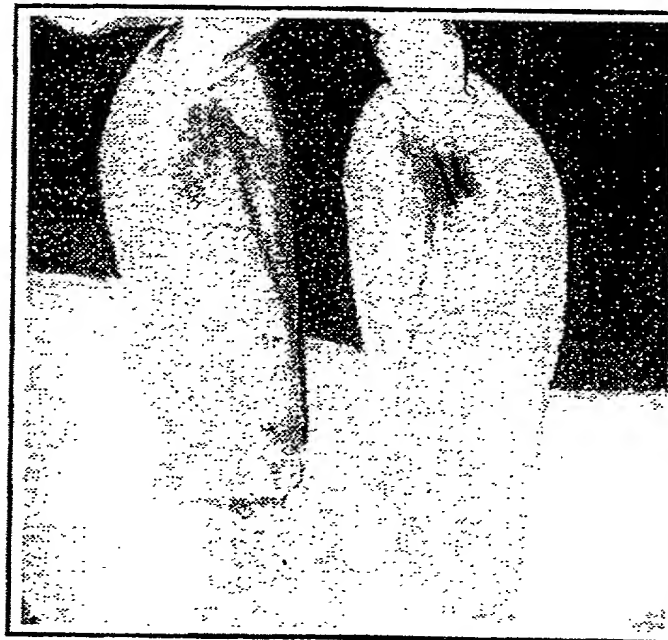


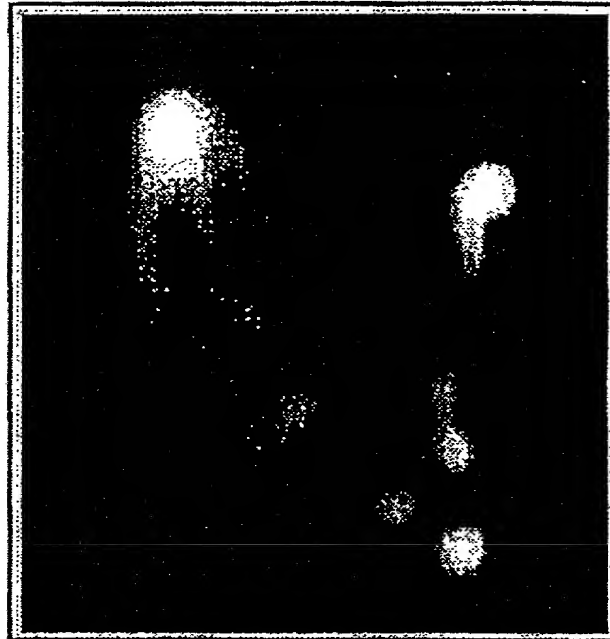
FIG. 17B

09/970,088-00000000



FIG. 17C

Control



VEGF-C



FIG. 17D

09/970,088-000507

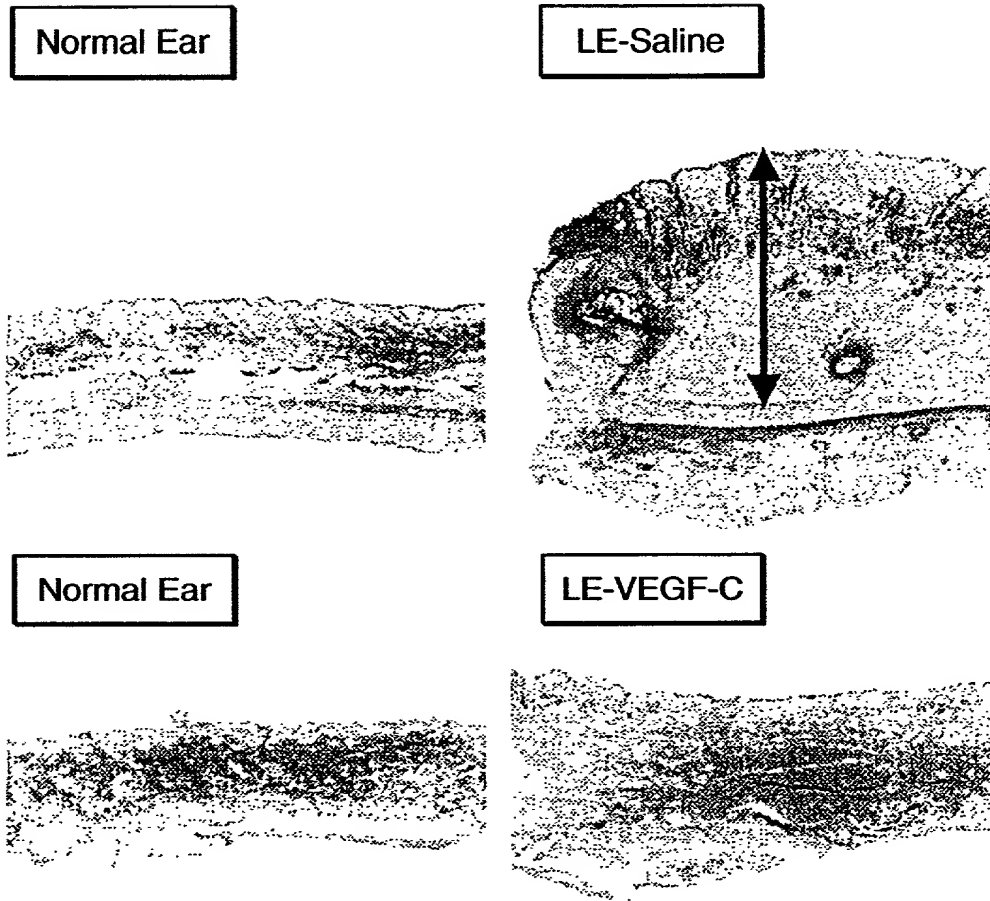


FIG. 18A

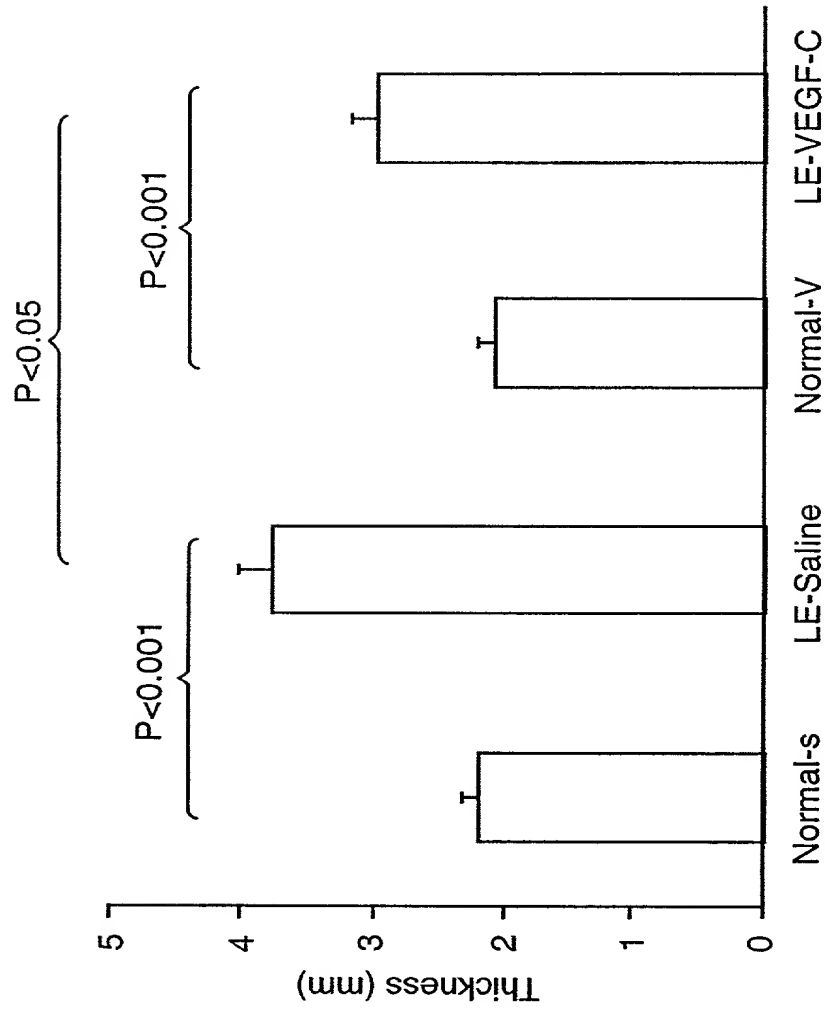


FIG. 18B



FIG. 19A

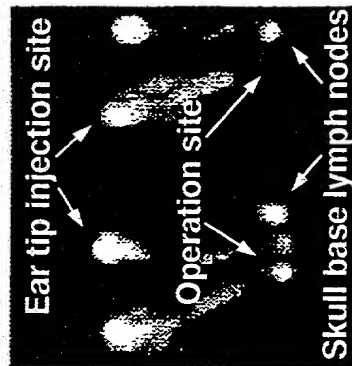
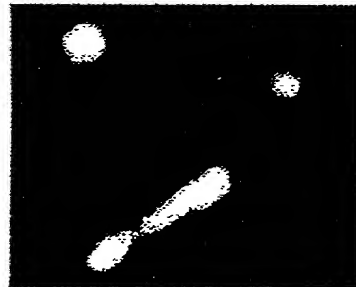
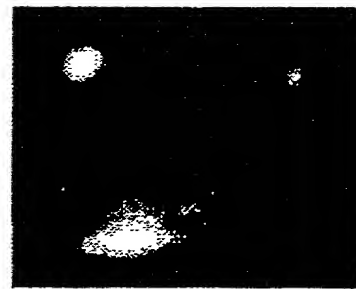


FIG. 19B



Saline

FIG. 19C



Saline

FIG. 19D



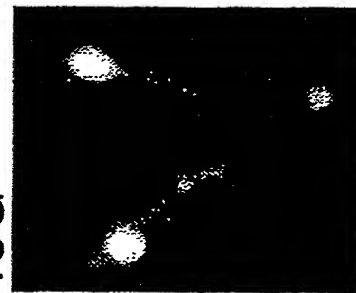
Saline

FIG. 19E



Saline

FIG. 19F



VEGF-C

FIG. 19G



VEGF-C

FIG. 19H



VEGF-C

FIG. 19I



VEGF-C

FIG. 19J

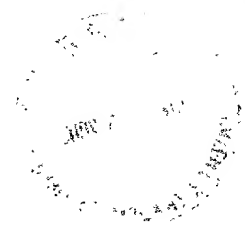
day 1

4 week

8 week

12 week

24/35



205030 8800/660

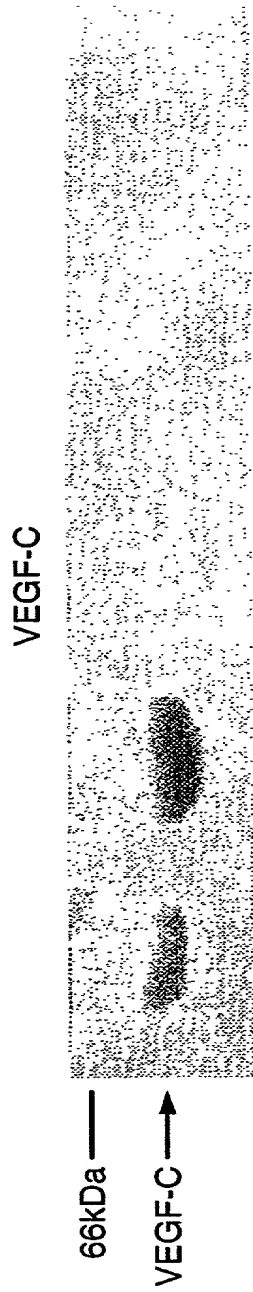


FIG. 20A

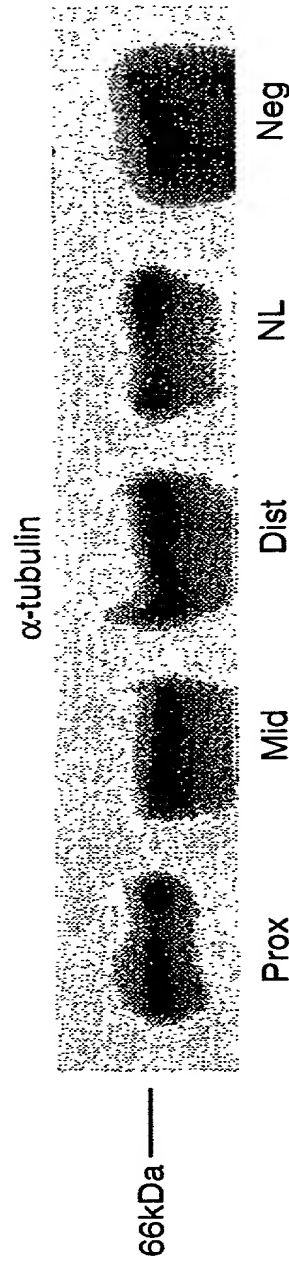


FIG. 20B

FIG. 21A
FIG. 21B

rb	1	CGGTGCGCGG	TGGCCGGGGC	ACACGTGCCC	AGCATCGTAT	GGTACAAAGA
bo	1	CGGTGCCCCAG	TGGCTGGGAC	GCAAGTACCC	AGCATCGTGT	GGTACAAAGA
hu	1	CAGTGCTTGG	TGGCCGGAGC	GCAAGCGCCC	AGCATCGTGT	GGTACAAAGA
mo	1	CGATGCCCCG	TGGCTGGAGC	GCATGTGCCC	AGTATTGTGT	GGTACAAAGA
rb	51	TGAGAGGCTG	CTGCAAGAAG	AATCTGGAAT	CGACCTCGCG	GACTCGAACC
bo	51	TGAGAAGCTG	CTGGAAGAAG	AGTCCGGAAT	CGACCTGGCG	GACTCGAACC
hu	51	CGAGAGGCTG	CTGGAGGAAA	AGTCTGGAGT	CGACTTGGCG	GACTCCAACC
mo	51	TGAAAGGCTC	CTGGAGAAAG	AGTCGGGAAT	CGACCTGGCA	GACTCCAATC
rb	101	AGAGGCTGAG	CATCCAGCGC	GTGCGCGAGG	AGGACGCGGG	CCGCTATCTG
bo	101	AGAGGCTGAG	CATCCAGCGC	GTGCGCGAGG	AGGACGCGGG	CCACTATCTG
hu	101	AGAAGCTGAG	CATCCAGCGC	GTGCGCGAGG	AGGATGCGGG	ACGCTATCTG
mo	101	AGAGGCTGAG	CATCCAGCGC	GTGCGCGAGG	AGGACGCGAG	TCGTTATCTG
rb	151	TGCAGCGTGT	GCAACGCCAA	GGGCTGCGTC	AACTCCTCCG	CCAGCGTAGC
bo	151	TGCAGTGTGT	GCAACGCCAA	GGGCTGTGTC	AACTCCTCTG	CCAGCGTGCG
hu	151	TGCAGCGTGT	GCAACGCCAA	GGGCTGCGTC	AACTCCTCCG	CCAGCGTGCG
mo	151	TGCAGCGTGT	GCAATGCCAA	GGGCTGCGTA	AACTCCTCTG	CCAGCGTGCG
rb	201	TGTGGGAGGC	GCCGAAGATA	GAGGCAGCAT	GGAGATCGTG	ATCCTCGTGG
bo	201	TGTGGAAGGC	TCTGAGGATA	AAGGCAGCAT	GGAGATCGTG	ATCCTTGTGT
hu	201	CGTGGAAGGC	TCCGAGGATA	AGGCAGCAT	GGAGATCGTG	ATCCTTGTGT
mo	201	AGTGGAAGGC	TCTGAAGATA	AAGGCAGCAT	GGAGATTGTG	ATACTCATTT

FIG. 21A

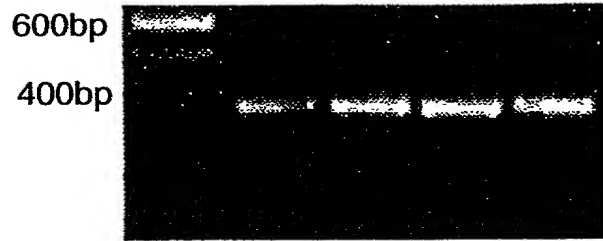
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rb	251	GCACCGGCGT	CATTGCCGTG	TTCTTTTGGG	TCCTCCTCCT	GCTCATCTTC
bo	251	GCACCGGAGT	CATCGCTGTC	TTTTTCTGGG	TCCTCCTTCT	CCTCATCTTC
hu	251	GTACCGGCGT	CATCGCTGTC	TTCTTCTGGG	TCCTCCTCCT	GCTCATCTTC
mo	251	GCACCGGCGT	CATCGCAGTT	TTCTTCTGGG	TCCTCCTCCT	GCTCATCTTC
rb	301	TGTAACATGA	GGAGGCCAGC	CCACGCGGAC	ATCAAGACGG	GCTACTTGTC
bo	301	TGTAACATGA	GGAGGCCAAC	CCATGCAGAC	ATCAAGACTG	GCTACTTGTC
hu	301	TGTAACATGA	GGAGGCCGGC	CCACGCAGAC	ATCAAGACGG	GCTACCTGTC
mo	301	TGTAACATGA	AAAGCCTGC	CCATGCAGAC	ATCAAGACGG	GCTACCTGTC
rb	351	CATCATCATG	GATCCCCGGG	AGGTGCCCTCT	GGAGGAGCAA	TGTGAATACC
bo	351	CATCATCATG	GATCCCCGGG	AGGTGCCCTTT	GGAGGAGCAG	TGTGAATACC
hu	351	CATCATCATG	GATCCCCGGG	AGGTGCCCTCT	GGAGGAGCAA	TGCGAATACC
mo	351	CATCATCATG	GATCCCCGGG	AGGTGCCCTTT	GGAGGAGCAG	TGTGAATACC
rb	401	TGTCCTACGA	CGCCAGCCAG			
bo	401	TGTCCTACGA	TGCTAGTCAA			
hu	401	TGTCCTACGA	TGCCAGCCAG			
mo	401	TGTCCTATGA	CGCCAGCCAG			

FIG. 21B

FIG. 22A

FIG. 22A



Mes Lung Kidney LN

FIG. 22B

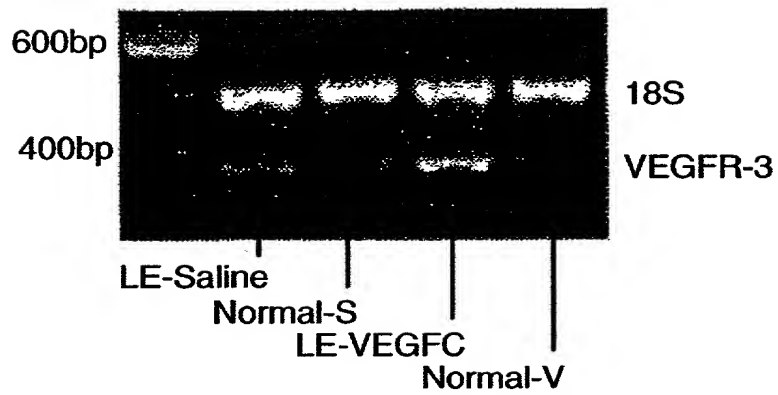


FIG. 22C

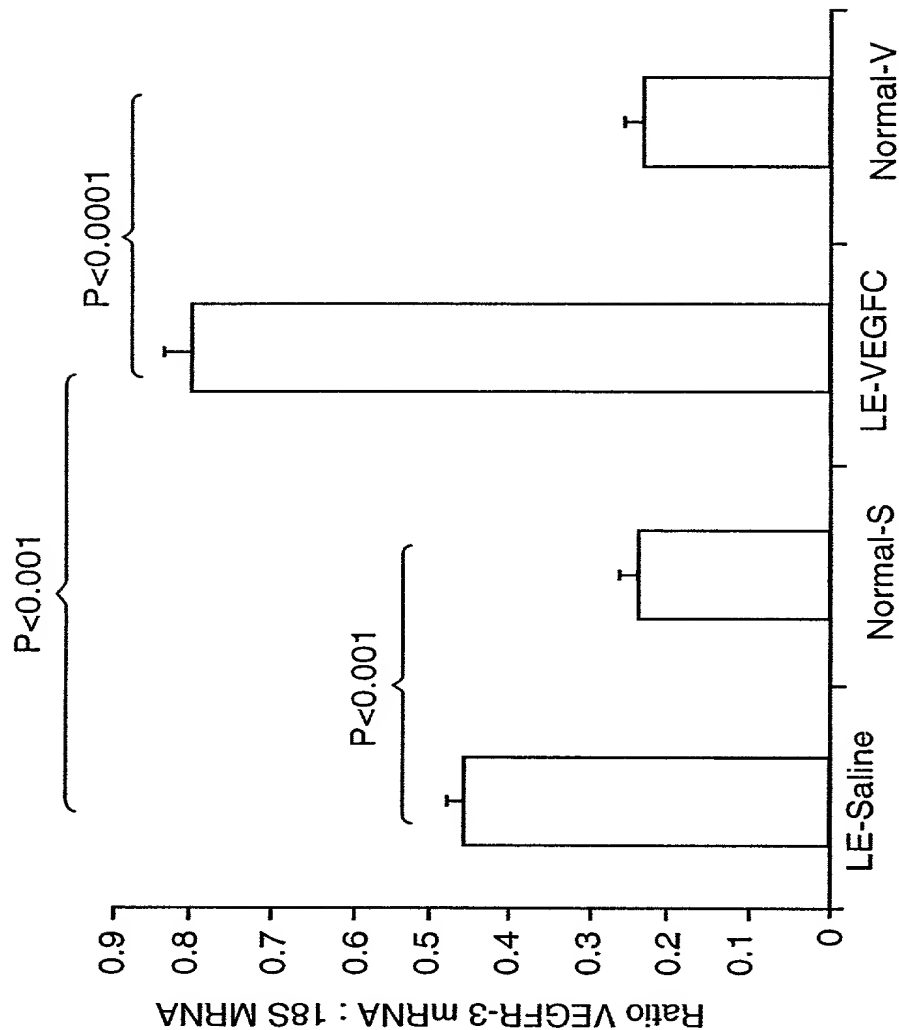


FIG. 22D

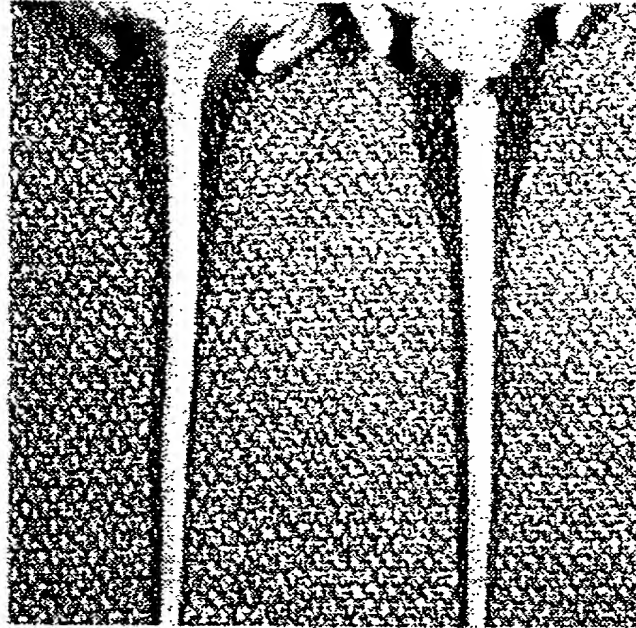


FIG. 23A

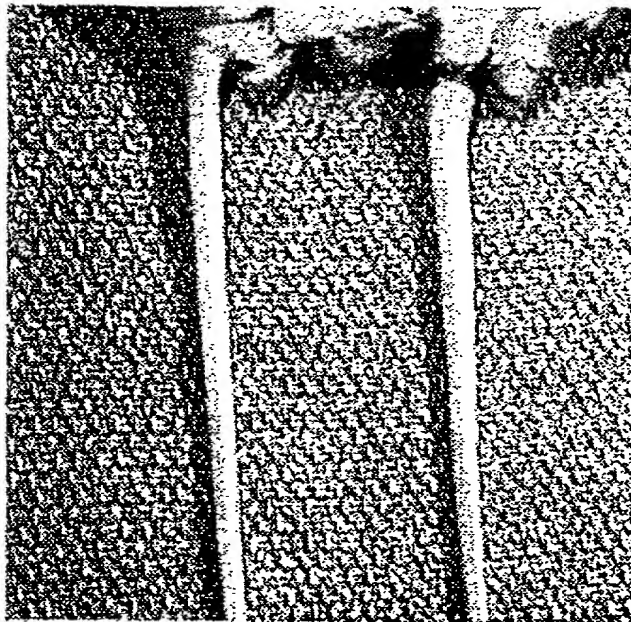


FIG. 23B

09970088-066502

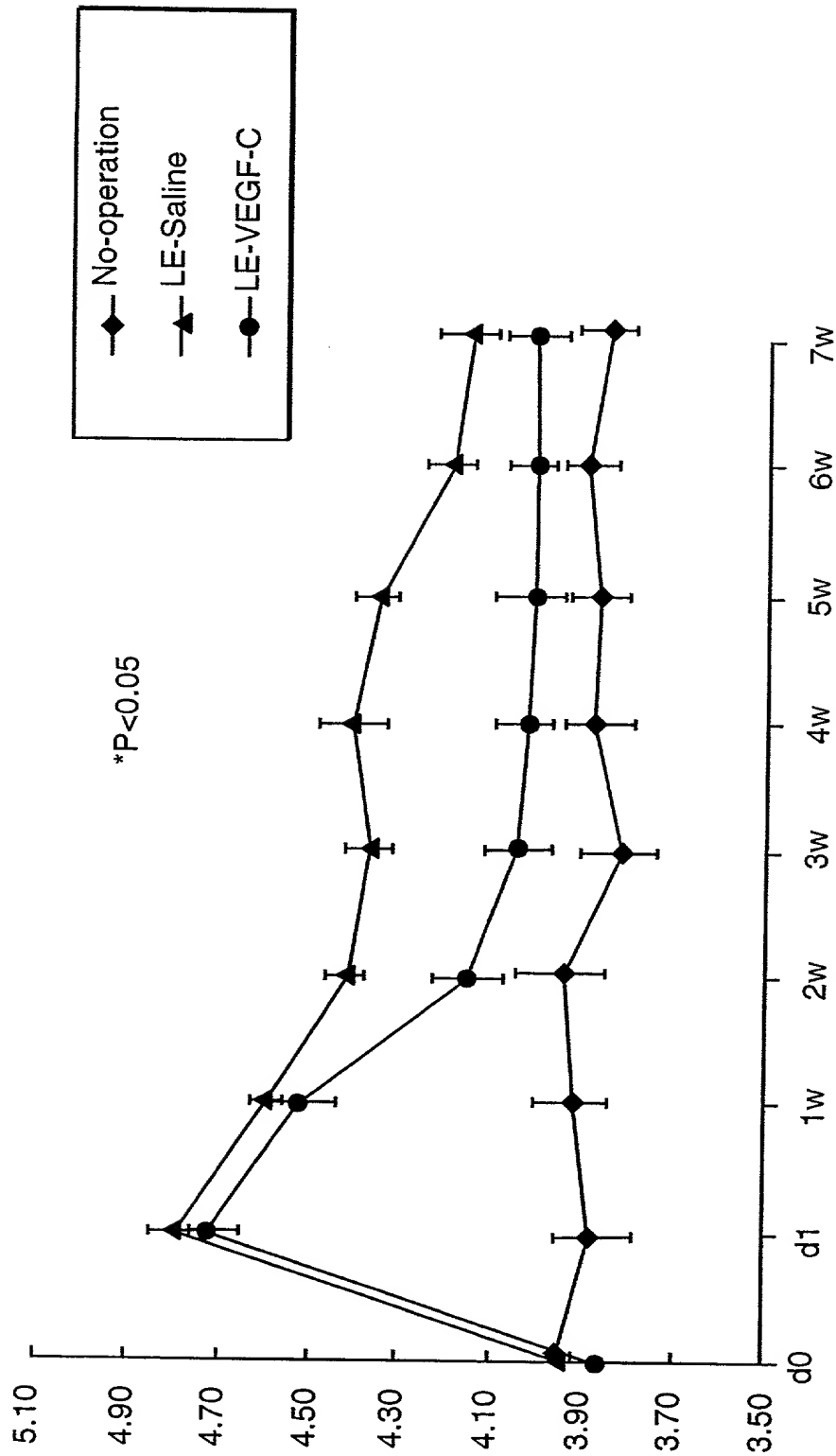


FIG. 23C

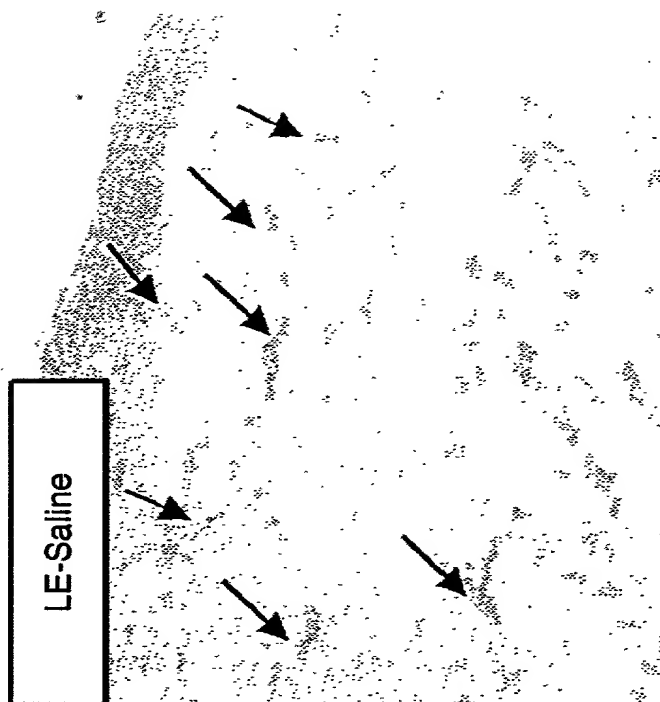


FIG. 24B

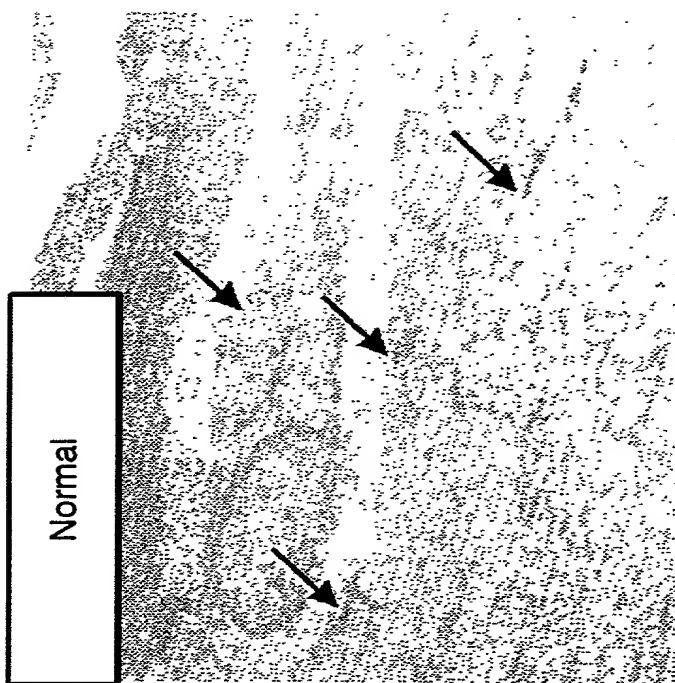


FIG. 24A

205090* 98002650

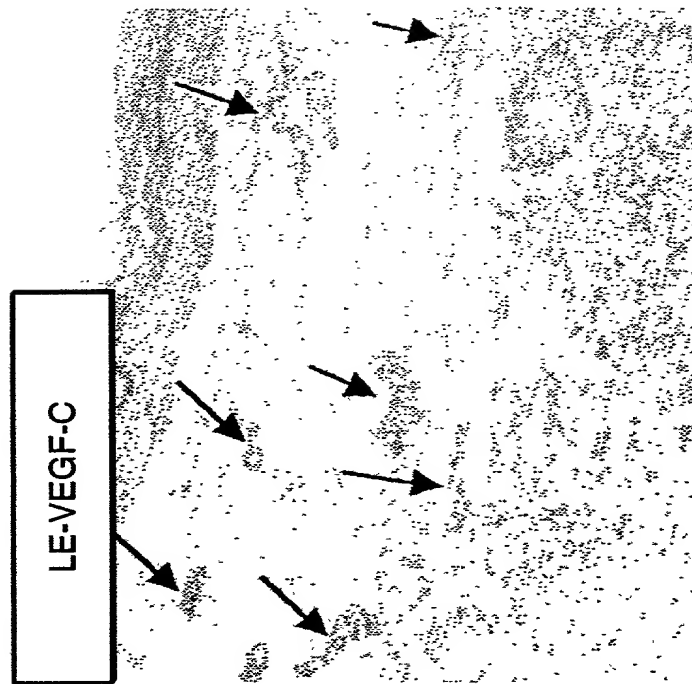


FIG. 24C

205000 8800 650

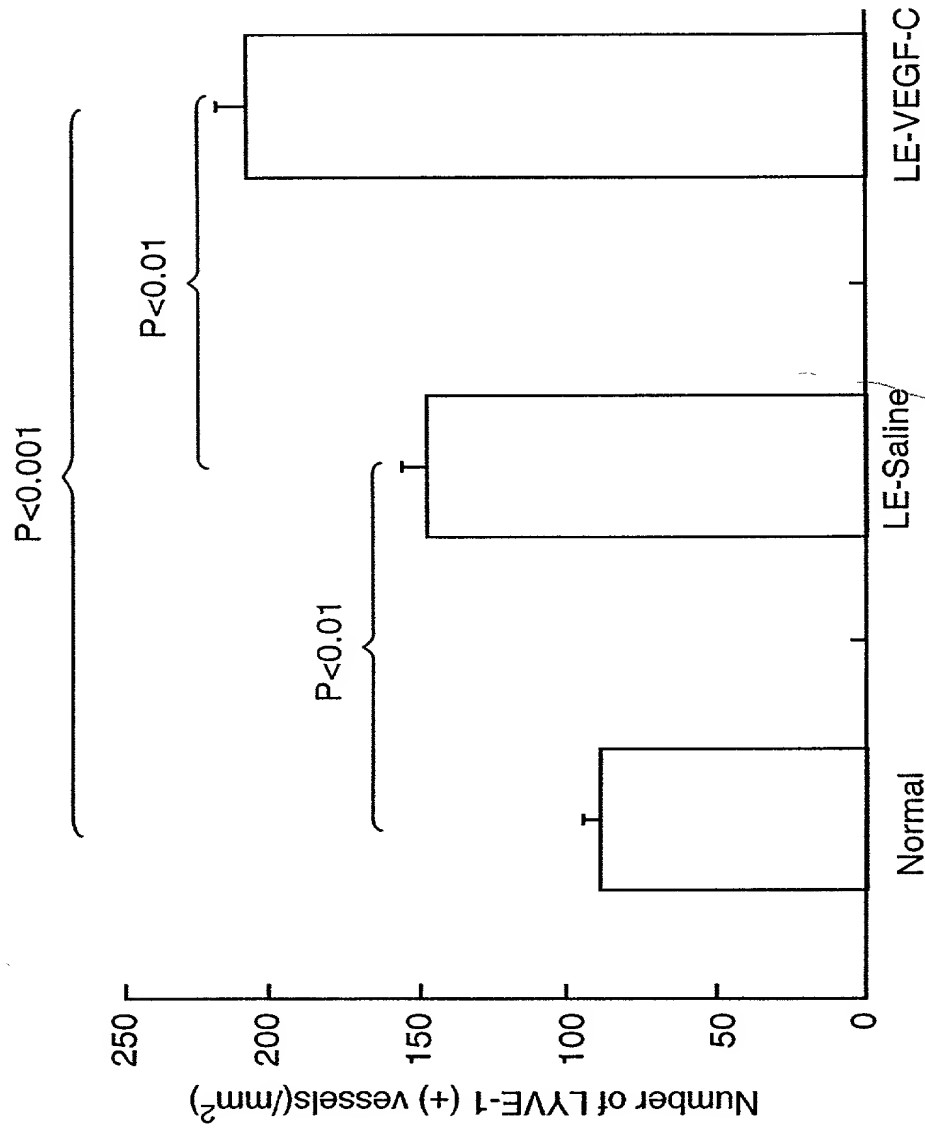


FIG. 24D